Paget's disease of the Bone:

There are Paget's disease of the bone and Paget's disease of the skin so we have to specify the type.

The normal process which occurs in the bone:

- There is bone deposition and bone resorption occurring in continuous process ,like shedding of the epithelium and renewal of the epithelium, like the recycling of the RBCs (destruction and reproduction)
- Sometimes it works according to body demand or according to the pressure. For example if there is a radicular cyst, there will be pressure from inside to outside, then there will be resorption from the inside and compensation deposition from the outside. So there is always continuous remodeling of the bone.

Diseased bone:

- If there is a disease, this remodeling is disorganized; patient has excess either bone deposition or bone resorption .

Paget's disease of the bone

In this disease, the osteoclasts are abnormal; there is abnormal function of the osteoclasts which will result in features that will be discussed.

So in Paget disease of the bone there is disorganized formation and remodeling of the bone (osteodystrophy).

What cause the osteoclasts to malfunction is unknown but theories and suggestions include:

- *Paramyxoviral infection* and latency; for example EBV latency in the B cells, here Paramyxoviral latency could be in the osteoclasts progenitor cells altering these progenitor cells producing abnormal osteoclasts. These osteoclasts will hyperfunction sometimes so there will be a lot of bone resorption and this will give radiolucent lesions followed by bone deposition and sclerotic areas of bone.
- *Genetic Predisposition* : as it was found to occur in certain group of people -in familial pattern- and in certain population like in United Kingdom.

  And a locus identified on the chromosome 18q –q means that it is on the long arm of chromosome 18-.

All of these are theories, there is nothing confirmed except the clinical features of the disease.

Pathogenesis:

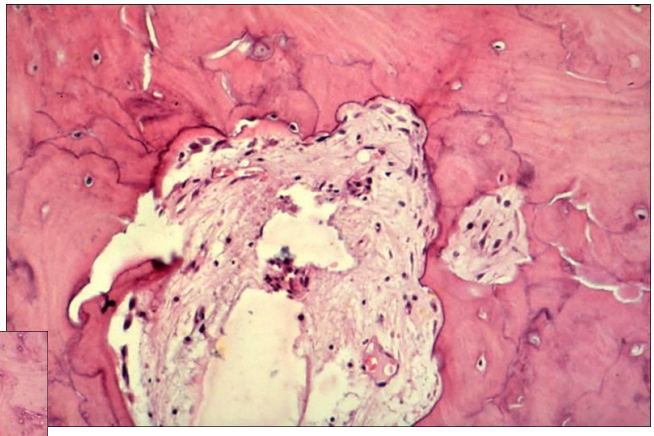
There are three overlapping phases, with no clear undercut between the phases.

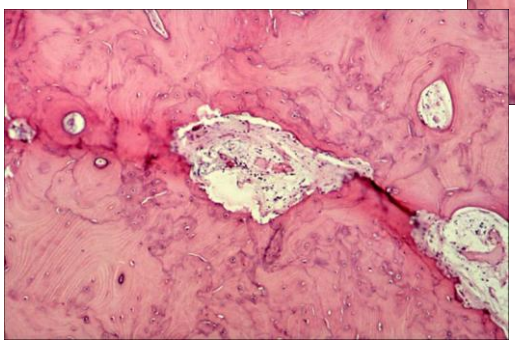
- First of all the osteoclasts will be over functioning eating a lot of bone producing radiolucent lesions (decreasing the radio-opacity). These spaces that made due to bone resorption will be filled with ***fibrovascular tissue.*** This tissue is very vascular having dilated blood vessels which will induce pooling of blood.

If a patient with heart failure having this disorder with a wide area of resorbed bone with a lot of blood vessels which are dilated and containing a lot of blood, then patient's heart will be impaired more and more because of pooling of blood inside the bone and this will increase the heart failure.

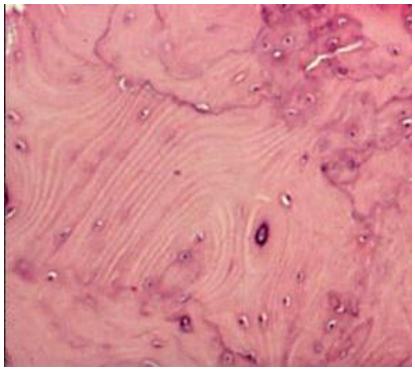
So the first stage due to increase osteoclasts activity there will be bone resorption.

The osteoclasts usually look like multinucleated giant cells and set in their own lacunae.





- The second phase is the active stage of ***mixed*** *osteolysis and osteogenesis* and microscopically there will be a lot of osteoclasts and osteoblasts.



- In the third phase the osteoclasts function will be stopped and the abnormal function will stop. Then there will be an increase in the deposition of the bone producing dense bone with decrease vascularity.

So first and third stages are opposite to each other; in the first stage there is osteolysis and a lot of vascularity but in the third phase there is osteosclerotic and decreases in the number of blood vessels.

The first phase will give the deformed architecture of the bone, the bone will be malformed or abnormal in shape. **But the third phase will stabilize the first phase**. So the deformity which occurred in the first and second phases will be stabilized by the third phase where deposition occurs.

If a tooth was extracted while the patient is in the first stage, there will be excessive or uncontrolled bleeding due to increase vascularity and the dilated blood vessels.

But extraction of a tooth in the third phase will be difficult and may be there will be *Ankylosis* due to *hypercementosis* and bone deposition leads to fracture as the bone is very brittle. Bone Infection is another complications , because there is decrease in the blood supply leading to increase bone infection tendency.

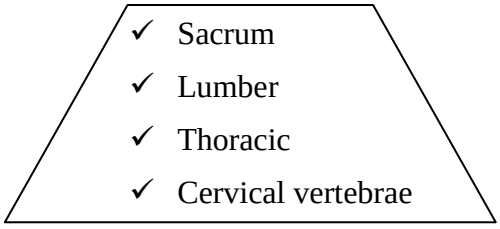
Patients affected by Paget's disease are usually elderly in 60s, but in general they are over age of 40.
And predominant in males.
The overall incidence is 3%.

There are geographic differences in incidence. It is more common in UK, Australia, and North America; may be due to certain genetic changes or familial predisposition or endemic areas of Paramyxoviral infection.

It is a chronic disease that has three phases overlapping over along period of time.

Bones which are commonly involved by Paget's disease:

- May involve a single or small number of bones
- Weight-bearing bones of the axial skeleton are the commonest



- The skull and femur are the next most frequent
- More common in Maxilla than Mandible

Bone deformity … in weight-bearing bones as body weight on femur and sacrum this will facilitate or increase **the bending** (deformity) of these bones due to bone resorption phase (*osteolytic*) and then there will be *Sclerotic phase* and kept in the same place (shape) . This deformity happens in the skull and maxilla also without clear physical explanation.

There will be bone pain and there is pathological fracture because the bone is brittle (very hard or dense). This bone pain may be because the new bone will induce pressure on the nerves within the bone itself causing pain.

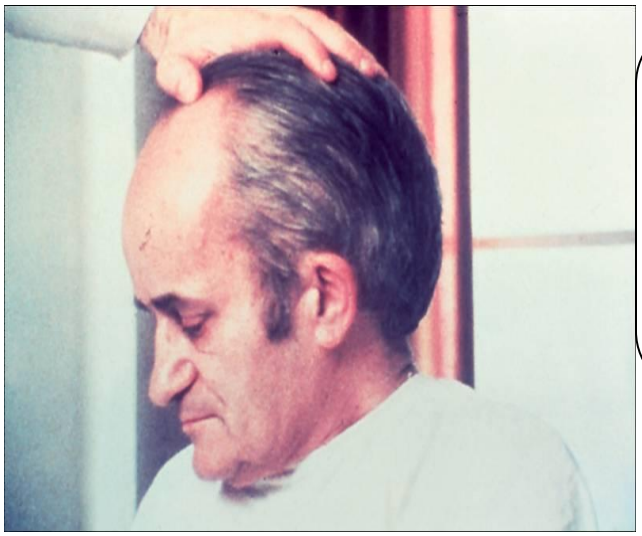
Complications of involving of the skull:

1- Neurological defects; may be the foramina of the ***cranial nerves*** will be constructed and there will be pressure on the nerves … neurological changes.

2- Facial nerve involvement … Facial nerve palsy.

3- Hearing impairment.

So according to the area involved.

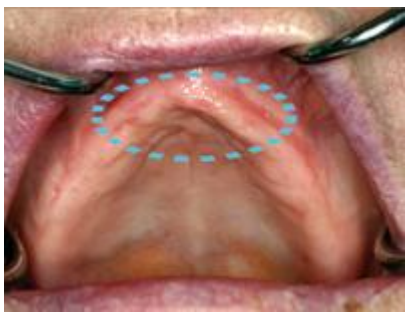


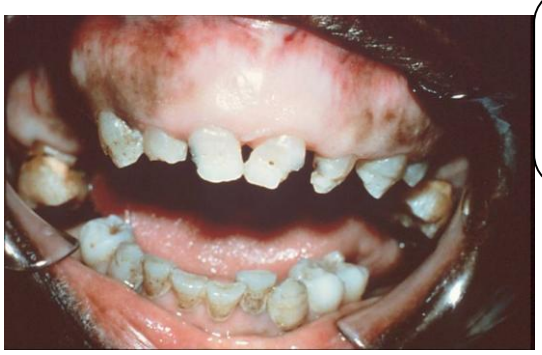
Skull itself will enlarge gradually.

In UK people use hats and the classical description is that the patient will have to change the hat several times in the year because patient head will increase in size so the hat will not fit his head.

Patient with complete denture will need to change the denture because the maxilla is enlarging.

The palate in edentulous patient will be enlarged and when it is enlarged it will be widened and flattened and the patient will need to change his complete denture regularly until stabilization occurs.





Enlargement of jaws mainly the maxilla. And when the bone is enlarged there will be spaces between the teeth and because the teeth are having a lot of spaces, teeth will be inclined palatally.

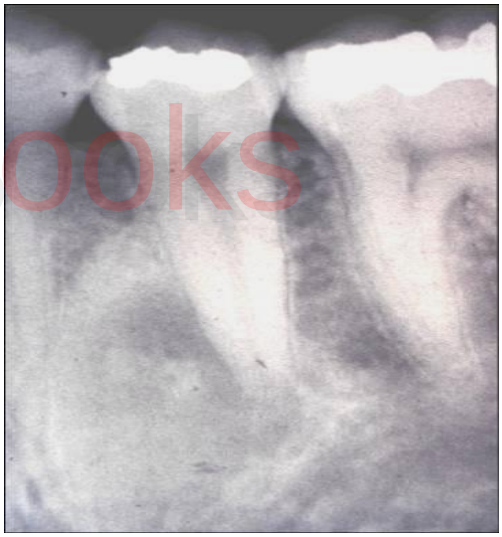
Narrowing of cranial nerve foramina may cause cranial nerve dysfunction.

Enlarging of the skull and facial bone in general.

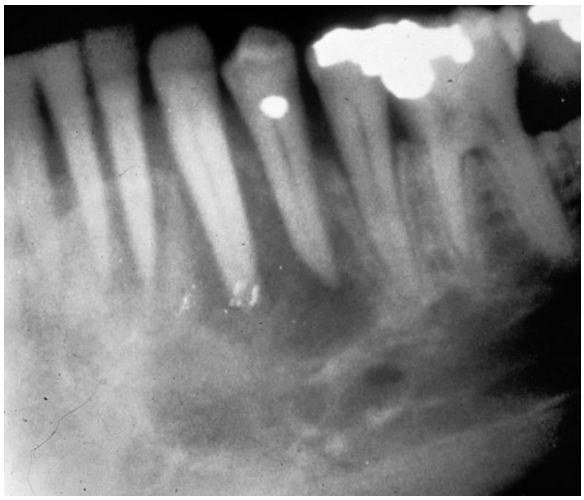
Facial deformity … general look of the patient will be changed and the derangement of occlusion because of space among teeth.

Oral features and teeth related features:

- Teeth may be ankylosed with hypercemenosis.
- No PDL can bee seen, the tooth is directly fused to the bone, so extraction of these teeth is difficult.
- Bone is very dense and this bone is hypervascularized so prone to infection due to extraction.



In the osteolytic phase may be widening of *lamina dure* space (PDL).

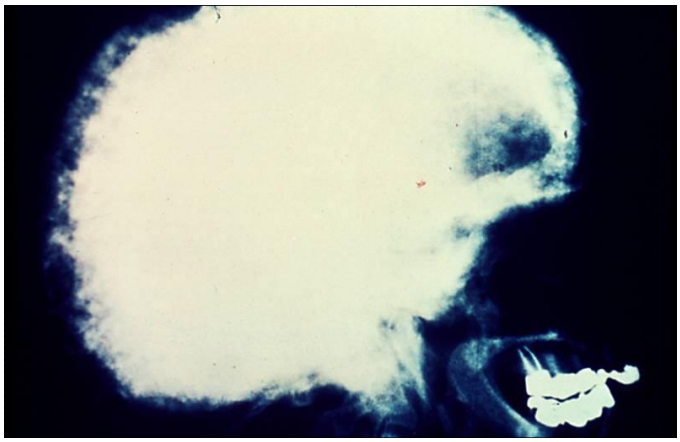


Hemorrhage is one of the complications of first stage but infection is a complication of the third phase.

Radiographic features :

In early phases when the bone resorption is the prominent feature, osteoporosis like features will be seen (density of bone decreased).

Later stages we will see something called "*cotton-wool appearance*". Cotton because it is very white.



Cotton-wool patches in the skull as they are very mineralized bone so very white and the diploe of the skull, the 2 plates will not be distinct due to bone resorption, bone deposition and malformation. So all disorganized.

Sometimes the outer plate is very thickened so you cant distinct where is the inner and where is the outer according to the stage of the disease.

Loss of diploe, outer plate not clearly identified, it is thickened but here I can say that this is the outer plate but in the other side we can't see outer and inner plate distinctly due to thickening of outer plate.

Microspically:

First phase; a lot of osteoclasts may be setting in lacunae …a lot of fibrovascular tissue in the bone marrow and dilated blood vessels … there will be reverse in the activity of the bone. First excessive resorption then resorption and deposition so when the reverse in activity occurs there will be reversal lines in the bone.

Reversal lines appear different in color compared to the surrounding bone and occur as the activity switches between deposition and resorption, mineralization of bone will be changed and the mineralization will be reflected as a change in color.

Cementum also may show this disorganized remodeling, *hypercementosis* and *ankylosis* and *osteosarcoma* may be a finding in Paget's disease.

Paget's disease of bone may be complicated by an aggressive malignant tumour of bone

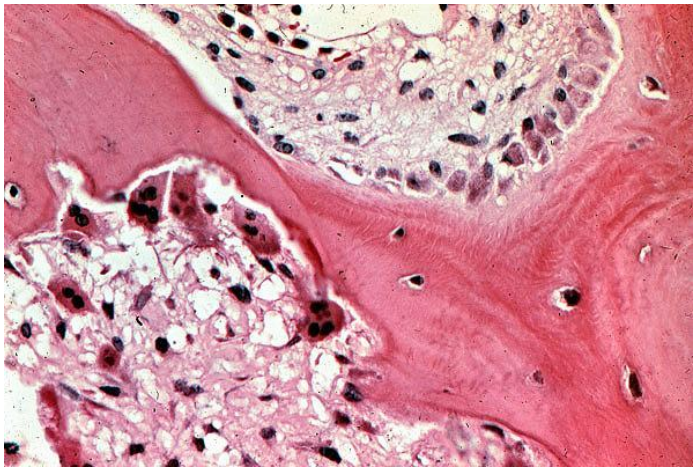
called *osteosarcoma*.

So patient with Paget's disease the biopsy should be examined in details looking for suspicious areas for malignancy.

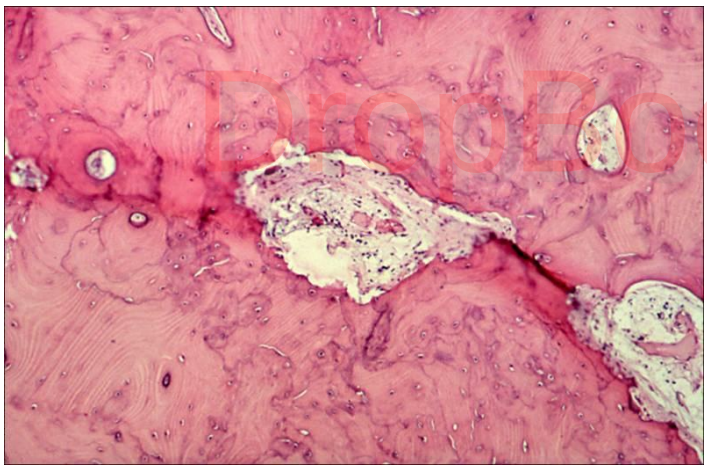
Lab studies:

Increased serum *alkaline phosphate enzyme* which is related to bone turn over and calcium and phosphorus will be normal may be slightly increased but usually they are within normal limits so the enzyme is elevated.

Fibrovascular tissue in the marrow spaces and here blood vessels, these are the lacunae of the osteoclasts may be multinucleated of flattened on the bone.



The very obvious feature is the presence of the reversal lines, these lines reflect or represent the switch of the activity of the bone from resorption to deposition leaving this area of altered mineralization may be called ***Mosaic lines***.



May be the second phase, there are dilated blood vessels but there is a lot of reversal lines and some single cell 'osteoblast' in their lacuna but there is big flattened cells with 2-3 nuclei.

Third phase: mainly scelerotic bone.

Treatment:

Some patient with multiple myeloma which is malignancy of plasma cells, they are being treated with *di-phosphonate* or *bis-phosphonate* which is also given to ladies with osteoporosis in post-menopause with *Calcitonin* to enhance deposition of bone and decrease bone resorption.

In multiple myeloma, the bone will be eaten by malignant plasma cells so there will be wide areas of resorption and back pain.

In patient with osteoporosis complications of fractures.

In Paget's disease syndrome, there is deformity in the bone due to bone resorption and changes.

So **di or bis – phosphonate** to decrease bone porosities but the complication is that sometimes it will induce sclerosis of the bone and the patient may come to the clinic complaining of osteomylitis (infection) due to decrease blood supply as the bone is sclerotic and there is complication of bone necrosis.

Complications:

Not fatal but has complications like increase incidence of osteosarcoma and other sarcomas (malignant neoplasms, malignant fibrous histiocytoma) 1% of patient get it, so it is not a small percentage.

Other complications:

- Heart failure
- Osteomylitis
- Hemorrhage special due to extraction
- fracture and bone pain.

Giant cell lesions of Bone:

We took peripheral Giant cell granuloma in gingiva, the differential diagnosis of epulis; peripheral giant cell granuloma, peripheral ossifying fibroma, pyogenic granuloma "3Ps".

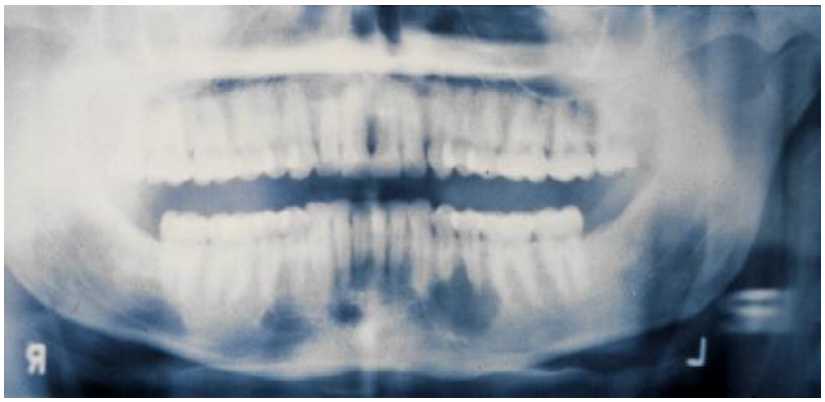
Peripheral giant cell granuloma has center counter bike called center giant cell granuloma which has multinucleated giant cells, fibrous like tissue and a lot of blood vessels, it is a vascular lesion "small blood vessels".

The behavior of center ginat cell granuloma not like a benign tumour, so it doesn't enlarge forever, it looks like a reactive lesion.

Central Giant Cell Granuloma could be a reactive lesion due to trauma and sometimes they said that there is a spectrum, if you remember the hemodynamic theory that the trauma for the mandible may induce stafen's bone cavity or idiopathic bone cavity which is an empty cavity at one end but the other end it may induce aneurysmal bone cyst which is filled with blood and may induce hemorrhage and bone expansion. This central giant cell granuloma most likely is a reactive lesion in the spectrum between these 2 ends.

So it is a reactive lesion, and not Neoplastic. It is reactive to hemodynamic change (Trauma or hemorrhage), non-aggressive which enlarge and induce expansion of the bone.

Most common in young adult, female predominant, only occurs in jaws, mostly in mandible 70%. Involves anterior part of the jaws. So the most affected area is the anterior part of the mandible.



This is an OPG and here we have anterior to premolar region in the mandible and it is radiolucent Unilocular in anterior part of the mandible.

Dr. Rima saw 2 cases with central giant cell granuloma both in young females in anterior part of the mandible and both associated with bone expansion causing swelling in anterior part of the mandible so with radiograph we find this lesion.

Different Diagnosis:

OKC – Simple bone cyst which give scalloping appearance – idiopathic bone cavity.

Clinical appearance:

Symptomless if non-aggressive and slow growing without perforation of cortex with low recurrence.

Swelling of the bone due to expansion caused by pressure from the inner aspect of the bone and bone deposition from the outer aspect.

Rapid growth most of it non-aggressive but some cases aggressive associated with pain and rapid expansion with loosening of the surrounding teeth with perforation of bone with high recurrence rate. So it needs treatment by block recession; removing a piece of the mandible to prevent recurrence of the aggressive lesions.

Radiographically:

Well-demarcated if non-aggressive or ill defined radiolucent area so poorly as it is aggressive.

Unilocular if it is non-aggressive and multinodular if aggressive. If multilocular but small locules is OK, sometimes after removal there is remnant which increase recurrence rate.

Can cause thinning, expansion or perforation of the cortical plate if it is aggressive and long standing.

Root displacement if the pressure inside the bone is low grade over along period of time so slowly growing mass so roots will have time to change its place.

Or root resorption if the mass is rapidly growing so it is a feature of malignancy; in osteosarcoma it induce root resorption so no time for the root to be displaced.

Not too much aggressive, it is ill-defined margins, 2 locules, but it is inducing displacement of root so it is chronic and may be long standing.

Microscopic features:

1- multinucleated giant cells, a lot of small size blood vessels so brownish due to hemosiderin and hemorrhage.

2- Fibrous CT, rounded, small or spindle.

Treatment:

Simple enucleation or curettage or aggressive treatment.

Recurrence:

15-20%

Long term prognosis is good and need to exclude hyperparathyroidism which induce brown tumour of bone; giant cell lesion similar to central giant cell granuloma.

So multiple giant cell granulomas mmediately check for hyperparathyroidism so we write this note for the clinician whenever we see a central giant cell granuloma.

Other giant cell lesions of the bone include:

Giant cell tumor of the bone:

This is different than the granuloma.

It is aggressive, it has a lot of giant cells, the number of the nuclei inside the giant cells is very high and it is very rare in the oral cavity so it is a true tumor.

So it is a True giant cell tumor of bone which is very rare in jaws, aggressive with high recurrence rate.

As it is tumor, it may metastasize.

So totally different compared with central giant cell granuloma and represent a true neoplasm.

Hyperparathyroidism:

Brown tumor of hyperparathyroidism called brown due to the color of the lesion that occurs in the bone of the patient with hyperparathyroidism. There will be bone resorption.

Parathyroid gland will try to elevate the calcium in the blood so when there is hyperparathyroidism there will be bone resorption to elevate the serum calcium level and the spaces in the area of the resorbed bone will be filled with multinucleated giant cells and fibrous tissue and blood vessels.

Because there are a lot of blood vessels, the RBCs when destroyed, they will release pigments and bilirubin so the appearance of the lesion will be brown and it is not the scientist brown or the pathologist it is just indication of the color.

Cherubism also has multinucleated giant cells.

Central giant cell granuloma has big multinucleated giant cells but the number of the nuclei is good not hundreds but in giant cell tumours there are hundreds of nuclei and the lesion is fibrous with small blood vessels filled with RBCs.

Done By :

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